“A STUDY ON SERUM AMYLASE LEVELS IN ACUTE ORGANOPHOSPHOROUS POISONING”

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MADURAI MEDICAL COLLEGE, MADURAI

CERTIFICATE

This is to certify that the dissertation entitled **"A STUDY ON SERUM AMYLASE LEVELS IN ACUTE ORGANOPHOSPHOROUS POISONING"** submitted by **Dr.T.JAMUNA DEVI** to The Tamilnadu Dr. M.G.R. Medical University, Chennai, in partial fulfillment for the award of Doctor of Medicine is a bonafide work carried out by her under my guidance and supervision during the academic year 2007-2008. This dissertation partially or fully has not been submitted for any other degree or diploma of this university or other.

DR.A.AYYAPPAN, M.D.,

PROFESSOR AND H.O.D.,

DEPARTMENT OF MEDICINE,

MADURAI MEDICAL COLLEGE

MADURAI.

DECLARATION

I**, Dr.T.JAMUNA DEVI**, solemnly declare that the dissertation titled **"A STUDY ON SERUM AMYLASE LEVELS IN ACUTE ORGANOPHOSPHOROUS POISONING"** has been prepared by me.

This is submitted to the Tamilnadu Dr.M.G.R. Medical University, Chennai, in partial fulfillment of the regulations for the award of MD Degree Branch I (General Medicine).

It was not submitted to the award of any degree/diploma to any University either in part or in full previously.

Place: Madurai
Date: **Dr.T.JAMUNA DEVI**

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CONTENTS

INTRODUCTION

1. INTRODUCTION

Acute poisoning by organophosphosphorous Pesticides (OP) has reached epidemic proportions in most parts of the world, particularly in developing agrarian countries, where the toxicity of available poisons and paucity of appropriate medical facilities ensure a high fatality rate.

Their ease of access and socio–cultural factors plays important role in choice of OP as a self-poison and the incidence is higher in young economically active group with a common fatality ratio of 20% [1,2].

According to WHO, world wide estimates of pesticide poisoning number 3 million each year, with 2 million hospitalized from suicide attempts and 2,20,000 deaths, the majority of which are actually intentional.

Poisoning due to occupational exposure, accounted for about one fifth of the incidents, with a fatality ratio of less than 1%. More than 90% of the non-occupational incidents were suicidal, with a fatality rate more than 10% and the majority of the subjects are young males.

Accidental exposures accounted for 8-10% of the incidents and homicidal use (less than 1%) were other forms of poisoning. The reported over all mortality following OP insecticide poisoning varies from 4-30% in different countries and institutions [4].

In India, OP compounds cause more self-poisoning deaths in southern and central India. In Northern India, aluminum phosphide causes most deaths with a fatality ratio

over 90%. Other Pesticides used for self –poisoning include carbamates, Organochlorines and pyrethroids. [5 Organophosphorous compounds are principally used as pesticides, and their exposure is highly prevalent in developing countries. Toxic effects of OPs are associated with significant morbidity and mortality and are a major global clinical problem.

Occupational, suicidal (or) homicidal exposure to OPs produces a characteristic but treatable syndrome in humans thus, early recognition and timely intervention of toxicity from these compounds are of great importance, to emergency physicians and patients.

Case reports on acute pancreatitis following acute organophosphorus compound ingestion has been reported now and then, but regular studies with reference to Pancreatitis is not available in a serial manner. Hence an attempt was made to study Pancreatic involvement through biochemical means.

REVIEW OF LITERATURE

2. REVIEW OF LITERATURE

➢ Origins of serum amylase :

A variety of organs and secretions contain amylase activity, including pancreas, salivary glands, fallopian tubes and cyst fluid, testes, lungs, thyroid, tonsils, breast milk, sweat, tears, and some malignant neoplasms. The pancreas and salivary glands contain amylase concentrations several orders of magnitude greater than other organs. Because large quantities of amylase are required to maintain the serum amylase level, it is unlikely that the other listed organs are important sources of amylase. This is demonstrated clearly in electrophoresis studies of normal serum. Electrophoresis shows that serum amylase is of 2 main types, as follows: (1) P-type amylase from the pancreas, and (2) S-type amylase from the salivary glands. Fallopian tube secretions, tears, breast milk, and sweat have amylases with a similar electrophoretic mobility of salivary isoamylase. However, the salivary glands account for almost all of the S-type isoamylase.

➢ Metabolic clearance of serum amylase :

The exact mechanisms of serum amylase metabolism are still not fully understood. Humans who have had a nephrectomy or have renal insufficiency have average serum amylase levels 50% higher than healthy individuals. Therefore, kidneys can be assumed to play a major role in amylase metabolism. However, kidney is not the sole organ responsible for amylase clearance in humans. The extrarenal mechanisms of amylase clearance have not been defined. Because of the high serum amylase levels also observed

in hepatic necrosis and cirrhosis, liver is thought to play a role in amylase metabolism.

- **Factors influencing serum amylase :**

Many conditions have been reported to cause hyperamylasemia. Although hyperamylasemia is commonly assumed to be due to the release of amylase into the serum by the diseased organ, the precise relationship between hyperamylasemia and an affecting condition is not entirely clear. Hyperamylasemia is most commonly a result of (1) pancreatitis or parotitis, (2) decreased metabolic clearance of amylase, or (3) amylase released from an involved organ.

- **CAUSES OF HYPERAMYLASEMIA:-**

Pancreatic diseases:

Acute or chronic pancreatitis is associated with increases in the P-type isoamylase. In acute pancreatitis, serum amylase is usually elevated 3-fold and then returns to normal by 3-7 days. Patients with pancreatitis associated with hypertriglyceridemia or those with considerable acinar cell injury due to previous episodes of pancreatitis or chronic pancreatitis may not exhibit hyperamylasemia. Other reasons for hyperamylasemia that are associated with pancreatitis are pseudocysts, pancreatic ascites, pancreatic trauma, and choledocholithiasis. Pancreatic trauma can be a result of blunt trauma, abdominal or retroperitoneal surgery, or endoscopic retrograde cannulation of pancreatic duct (ERCP). Trauma related to ERCP is thought to result from the regurgitation of amylase into the blood, which may occur in 75% of ERCPs, but most have no evidence of pancreatic

injury. A 3- to 4-times increase in serum amylase levels 4 hours after ERCP predicts the occurrence of complicating postprocedure pancreatitis. In patients presenting with biliary-type abdominal pain, a 3-fold increase in serum amylase levels that returns to normal within 48-72 hours suggests stone passage through the common bile duct.

Salivary diseases:

Parotitis is associated with increases in the S-type isoamylase. Parotitis is usually caused by trauma or surgery to the salivary gland, radiation to the neck area involving the parotid gland and subsequently causing duct obstruction, or calculi of the salivary duct. Another cause of damage to the salivary gland is from chronic alcoholism. Salivary amylase levels are 3 times higher than normal in 10% of patients with alcoholism; this may be related to chronic liver disease.

Decreased metabolic clearance:

Renal failure results in increased S-type and P-type isoamylases. Liver disease from hepatitis or cirrhosis also results in increased S-type and P-type isoamylases.

Macroamylasemia

Macroamylasemia is a benign condition where the amylase molecule binds with a large complex molecule (e.g., immunoglobulin, polysaccharide), thereby prolonging its half life and decreasing renal clearance. About 2-5% of patients with hyperamylasemia have macroamylasemia.

Intestinal disease:

Gut diseases, including mucosal inflammatory disease of the small intestine, mesenteric infarction, intestinal obstruction, appendicitis, and peritonitis, usually result in increased P-type isoamylase because of increased absorption of amylase from the

intestinal lumen. Gut perforation leaks the contents into the peritoneum causing inflammation and absorption of amylase across the inflamed peritoneum. This can result in hyperamylasemia.

Female reproductive tract disease:

Ruptured ectopic pregnancy, fallopian or ovarian cysts, and salpingitis can result in increased S-type isoamylase.

Miscellaneous causes:

Ectopic amylase production by lung, ovary, pancreas, and colon malignancies; pheochromocytoma; thymoma; multiple myeloma (increased salivary amylase); and breast cancer (increased pancreatic amylase) are miscellaneous causes of hyperamylasemia.

Acidosis, which can be due to (1) ketoacidosis that results in increased S-type and P-type isoamylases or (2) nonketotic acidosis that results in increased S-type isoamylase, can cause hyperamylasemia.

Amylase increases may occur postoperatively, resulting in increased S-type and P-type isoamylases; however, an increase in salivary amylase is more common. This may occur after extracorporeal circulation or nonabdominal surgery (e.g., 30% of patients undergoing cardiac surgery have elevated S-type isoamylase).

Other causes of hyperamylasemia include pneumonia (increased salivary amylase), cerebral trauma, burns, abdominal aortic aneurysms (increased pancreatic amylase), drugs (increased salivary and/or pancreatic amylase), anorexia nervosa and bulimia (increased salivary amylase), and organophosphate poisoning.

Rare cases of hyperamylasemia are reported in association with systemic lupus

erythematosus (SLE), as well as ciprofloxacillin treatment.

- **LABORATORY SIGNIFICANCE :**

The most widely used application of serum amylase measurements is to support a diagnosis of acute pancreatitis. In acute pancreatitis, the serum amylase is increased at least 3-fold in approximately 75% of cases on the initial day of symptoms; then, it usually returns to normal by 3-7 days. The specificity of the test increases with higher levels of the enzyme.

Serum amylase measurements are not very sensitive or specific for pancreatic injury because they may be normal in patients with preexisting acinar injury or chronic pancreatitis and because many other causes of hyperamylasemia are described earlier. One should remember that a patient with asymptomatic chronic hyperamylasemia almost never has pancreatic disease as the cause of the amylase elevation. In cases of mild elevations of serum amylase, other methods may be used to help determine the cause of hyperamylasemia.

The amylase-to-creatinine clearance ratio (ACR) can help differentiate acute pancreatitis from other conditions. This ratio is calculated using the following equation:

ACR = (amylase[urine] X creatinine[serum]) / (amylase[serum] X creatinine[urine])

X 100

An ACR of greater than 5% suggests acute pancreatitis. However, the ACR is also known to be increased in diabetic ketoacidosis and renal disease and after surgery. An ACR of less than 1% suggests macroamylasemia. Because findings of urinary amylase are relatively nonspecific, calculations for urinary amylase excretion have almost no clinical value. Generally, the ACR measurement has been abandoned, except to confirm a diagnosis of macroamylasemia,which is characterized by a low ACR. A lipase-to-amylase ratio of greater than 2 may suggest alcoholic pancreatitis, but it is not a reliable predictor of alcoholic pancreatitis.

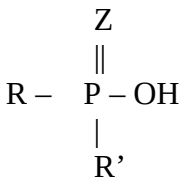
Serum isoamylase measurements to determine S-type isoamylase, P-type isoamylase, or macroamylasemia are the best tests to use when the etiology of hyperamylasemia is obscure.

2.1. ORGANOPHOSPHATES – A BACKGROUND

The clinical manifestations of OP Poisoning are caused by excessive synaptic accumulation of acetylcholine (ACh). OP compounds, irreversibly inhibit the enzyme cholinesterase (ChE) resulting in excessive accumulation of ACh, leading to the paralysis of cholinergic transmission in the CNS, autonomic ganglia, parasympathetic nerve endings, some sympathetic nerve endings and neuromuscular junctions.

Basic structure

The anticholinesterase Organophosphate compounds (OPs) are the organic derivatives of phosphorous containing acids, with a basic structure of,



R= alkoxy group (methoxy (or) butoxy)

R'= alkoxy (or) phenoxy group

Z = Oxygen (or) sulfur

Toxicokinetics

OP agents and carbamates are generally highly lipid soluble and hence may be systemically absorbed and can cause toxic effects within minutes after exposure. They are well absorbed by inhalation, occular exposure, across any mucosal surface, the skin and throughout the gastrointestinal tract (GIT). Skin exposure is extremely important, as many cases of toxicity occur after cutaneous exposure alone.

The onset, severity and duration of poisoning is determined by the degree, route of exposure, the lipid solubility and rate of metabolism of the particular compound and activation in liver, required before the compound is active.

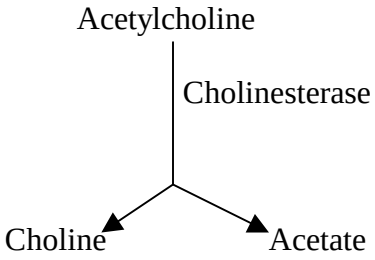
Direct acting OP agents function to inhibit cholinesterase directly, and do not require bio-activation in the liver. Indirect inhibitors require oxidation by the G1 mucosa and liver to active forms, which then inhibit ChE. Most of the commonly encountered insecticides such as Malathion and Parathion are indirect agents and require bioactivation

before manifesting toxicity. The onset of clinical effects may be from 5 min to 24 hours post exposure.

Because OP agents are very fat soluble they may accumulate in the body's fat stores which acts as a *"reservoir"*, prolonging elimination and toxic effects. This has been reported for more lipophilic compounds such as Fenthion and Chlorfenthion.[3].

2.2. CHOLINESTERASE (ChE)

Cholinesterase is one of the many enzymes needed for the proper functioning of the nervous system. It hydrolyses the ACh into choline and acetate .The choline formed is then recycled [7].



Types of ChE

- A specific acetylcholinesterase AChE (or) true cholinesterase: - Found primarily in nervous tissue and erythrocytes.
- Non – specific butyrylcholinesterase (BuChE) or pseudocholinesterase: - Present in plasma (or) serum and non- neuronal tissues [7].
- Brain cholinesterase.

The pathological effects of organophosphates result from inhibition of ChE [both, RBC and pseudocholinesterase]. These are the markers of exposure, acute toxic effects and reflect actual activity at cholinergic nerve terminal [11].

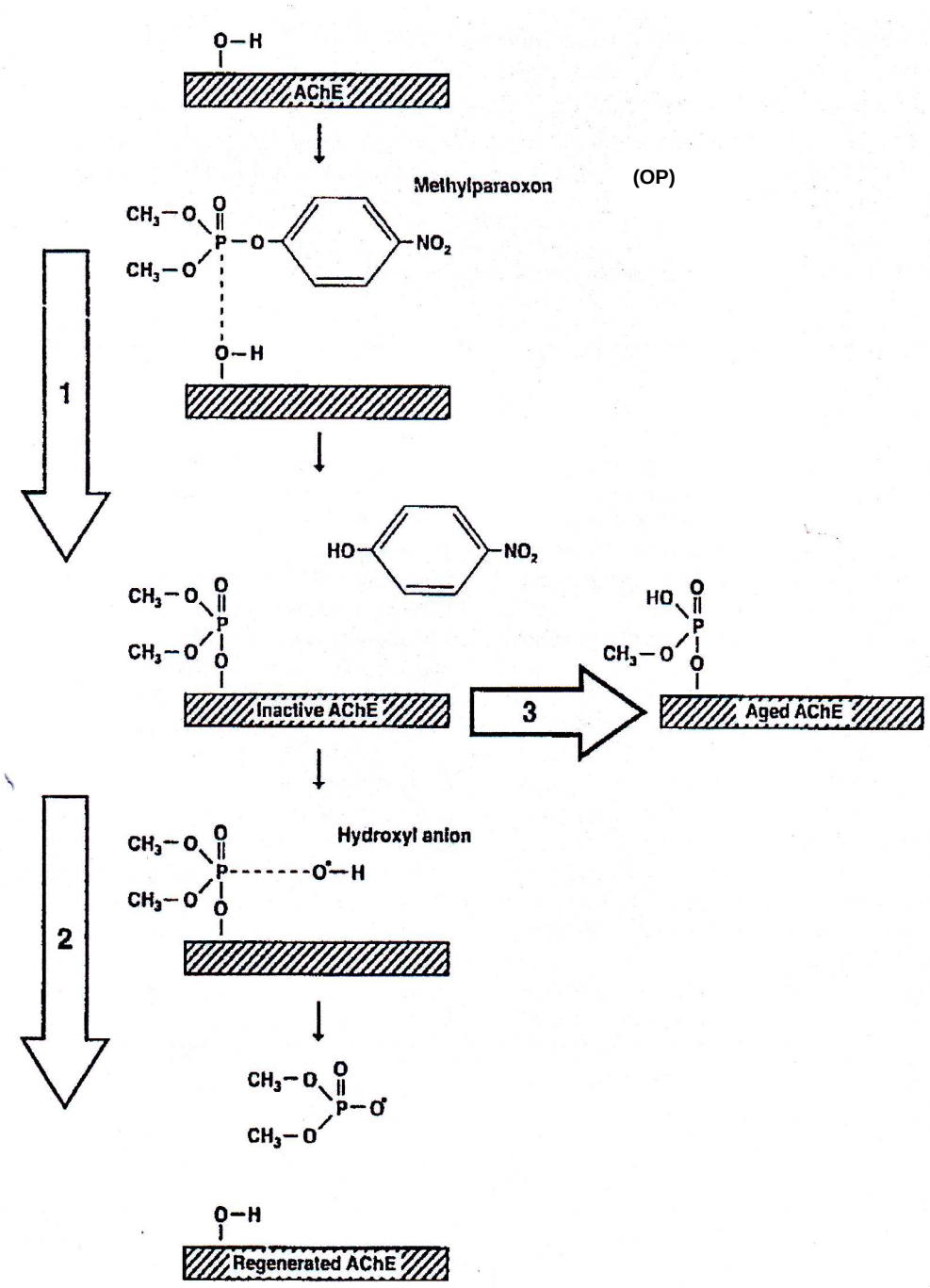
In the acute phase of OP poisoning serum ChE activity is usually depressed with in a few hours to few days and is also restored to normal levels quickly. About 3% of the population has a genetic variation manifested by a serum ChE deficiency. Pregnancy, acute (or) chronic inflammatory conditions, malnutrition and liver disease are conditions that also affect serum ChE levels, but the depression caused by these conditions is not as great as that caused by organophosphate insecticides.

This level can vary widely from person to person. A 50% reduction in ChE activity from the baseline may result in acute cholinergic symptoms of organophosphate exposure. These values differ among laboratories, and the range is very wide, with a 30% spread [35].

Pathophysiology of OP poisoning

OP pesticides inhibit AChE at muscarinic and nicotinic synapses by depositing a phosphory1 group at the enzymes active site to form a temporary covalent bond, this results in an accumulation of ACh and uncontrolled activation of cholinergic synapses. Over time, one of two processes will occur. The covalent bond may spontaneously cleave leaving the enzyme functional again. This process may take up to 1,000 hours. Mean-while, the enzyme is prone to "*Ageing*" in its active state in which one of the "R" group may cleave non-enzymatically, leaving a hydroxyl group in its place. 'Aged' AChE with

its negatively charged phosphate can no longer be attacked by a negatively charged nucleophile, i.e. OH or an oximate group, and regeneration is no longer possible. Recovery of a functional pathway must wait until new ChE enzyme is manufactured, a process that may take weeks. This can take up to 3 months for RBC and several weeks for plasma ChE. The time it takes for ageing to occur varies according to the specific pesticide, but takes no longer than 48 hrs, Clinically, toxic effects of OP agents may persist more than a week[1,3].Oximes slows down “ageing” of the phosphorylated cholinesterase and binds to the OP agent, making it non reactive. This results in ChE regeneration and a rise in serum levels of ChE [11].



Mechanism of action of OP on AChE

Reactions

1. Inhibition of AChE by depositing a phosphoryl group at the enzyme's active site.
2. Regeneration of inactivated enzyme by removal of phosphoryl group.
3. Ageing of inactive AChE.

2.3. CLINICAL MANIFESTATIONS [3]

Table.4. List of the primary sites and clinical effects caused by excess Ach stimulation

PARASYMPATHETIC SYSTEM	CENTRAL NERVOUS SYSTEM	SKELETAL MUSCUES
Termed "Muscarinic"	Termed "nicotinic".	
Low Heart Rate	Delirium	Muscle weakness
Bronchospasm	Agitation	Muscle Fasiculations
Excessive oral secretions	Seizures	Muscle Rigidity
Excessive Tearing	Syncope	Muscle paralysis.
Vomiting	Apnoea	
Diarrhoea	Dizziness/ vertigo	
Abdominal cramping	Lethargy	
Salivation	Hypotension	
Sweating	Hypertension	
Constricted pupils (miosis)		

In recent works, it has been reported children, particularly those under nine years of age, are unlikely to develop classic "muscarinic" signs of OP poisoning. More often than not, younger children manifest "nicotinic" signs of poisoning. The most common features in pediatric poisoning are CNS depression and hypotonia [3].

Triphasic syndrome following OP poisoning

There are three distinct phases following OP poisoning.

i) – Initial Acute cholinergic crisis

ii) – Intermediate syndrome (IMS)

iii) – Delayed polyneuropathy

i) Acute cholinergic crisis:

Accumulation of ACh occurs at nerve endings as AChE is inhibited leading to '*cholinergic crisis'*, in which there is an initial stimulation and eventual exhaustion of cholinergic synapses. The clinical findings are a mixture of muscarinic effects resulting from the post ganglionic parasympathetic activity, nicotinic effects resulting from the accumulation of ACh at neuromuscular junctions and consequent depolarization and CNS effects causing initial excitation and subsequent inhibition of all CNS activity.

The Muscarinic symptoms of cholinergic excess are described by two common mnemonics.

DUMBELS	**SLUDGE / B B B.**
- **D**iarrhoea	- **S**alivation
- **U**rination	- **L**acrimation
- **M**iosis	- **U**rination
- **B**ronchorrhoea	- **D**efecation
- **B**ronchospasm	- **GI** symptoms
- **B**radycardia	- **E**mesis
- **E**mesis	- **B**ronchorrhoeea
- **L**acrimation	- **B**radycardia
- **S**alivation	

Patients may have hypertension and tachycardia occurring due to 'nicotinic' actions rather than hypotension and bradycardia. The nicotinic receptors activated during acute intoxication lead to muscle paralysis. Fasciculations may be seen and are a reliable sign of poisoning.

Severe intoxication may cause emotional irritability, mental obtundation, cognitive impairment, coma and convulsions because of CNS effects. In the cholinergic phase, paralysis usually passes off with in 48–72 hrs, but complete clinical recovery may take up to a week after exposure to these compounds [13].

ii) Intermediate Syndrome (IMS)

After the acute cholinergic phase, a second stage of weakness occurs 1-4 days later with (or) without a symptom free interval, and if left unrecognized, can lead to fatal respiratory depression.

IMS develops 12- 96 hours later exposure and reflects a prolonged action of ACh on the nicotinic receptors. The clinical features are muscular weakness in the occular, neck, bulbar, proximal limb and respiratory muscles with occasional dystonic posturing, requiring mechanical ventilation in an intensive care unit for several days[17].

The Respiratory failure may be due to aspiration of gastric contents excessive secretions, pneumonia and septicemia complicating adult respiratory distress syndrome[18]

The cranial nerve palsies are common. The sensory functions characteristically remain normal and full recovery is evident in 4-18 days.

The incidence of IMS in different studies has been reported to be between 20-68% and has been commonly associated with OPs, like Diazinon, Dimethoate, Methyl parathion, Methamidaphos, Monocrotophos, Fenthion and Ethyl parathion.

The development of IMS might be due to a conformational changes in the acetylcholine receptor altering the depolarizing neuromuscular block to a non – depolarization block, characterized by a fade on tetanic stimulation [45].

iii) Organophosphate – Induced Delayed Polyneuropathy (OPIDPN)

OPIDPN is a less common clinical condition which occurs within a period of one week to 5 – 6 months of the ingestion of an OP compound, almost exclusively in patients with preceding acute cholinergic toxicity. It is not associated with death but causes disability due to peripheral muscle weakness, recovery from which is not certain.

The neuropathy in OPIDPN is typically a symmetrical sensorimotor neuropathy with a distal predominance. Initial symptoms are paresthesia in the lower limbs and pain in the calves followed by motor involvement of the lower limbs, manifested by leg weakness, foot drop and muscle hypotonia. OPIDPN is motor predominant, and pure sensory neuropathy do not occur [9].

OPIDPN might be due to phosphorylation of an enzyme Neuropathy Target Esterase (NTE) in the nerve tissue resulting in neurological dysfunction. Modification of the structure of NTE initiates an irreversible polyneuropathy. This phosphorylated enzyme also undergoes ageing [4].

Table 3. Classification of Severity in Organophosphorous Poisoning (NAMBA) [9

Type of poisoning	Clinical definition
LATENT POISONING NAMBA – I	No clinical manifestations, Diagnosis depends on the estimation of SChE activity which is inhibited by 10-50%
MILD POISONING, NAMBA –II	The patient can walk but complains of Fatigue, head ache, dizziness, numbness of extremities, nausea and vomiting, excessive sweating and salivation, tightness in chest, abdominal Cramps or diarrhoea; SChE activity is 20-50% of normal value.
MODERATE POISONING NAMBA – III	The patient cannot walk and there is generalized weakness, speaking difficulty, muscular fasciculations, miosis and severe symptoms described above; SChE activity is 10 -20% of normal value.
SEVERE POISONING NAMBA IV	Unconsciousness, marked miosis and loss of pupil reflex to light, muscular fasciculations, flaccid paralysis, secretions from the mouth and nose, moist rales in the lungs respiratory difficulty and cyanosis; SchE activity is lower than 10% of normal value.

2.4. LABORATORY INVESTIGATION

Diagnosis of cholinergic excess is largely clinical and requires early recognition of the syndrome and a highly observant clinical setting.

1) Serum and Red Blood cell ChE activity

To confirm the exposure to an OP agent and to monitor prognosis of the patient. A 50% reduction in the activity of the enzyme is considered confirmatory for OP poisoning. An incremental response in enzyme activity is seen with treatment.

2) Serum electrolytes, creatinine and urea

To assess the degree of volume depletion in the presence of muscarinic secretory losses from the pulmonary and alimentary tracts [[15]].

3) Blood Urea Nitrogen (BUN) Monitoring

To predict the development of relapse in OP poisoning. Elevation from its normal range [8-20 mg/dl] is seen in acute poisoning [[16]].

4) Arterial Blood Gas (ABG) analysis

To assess the degree of hypoxia and / or hypercapnia in the presence of respiratory distress from pulmonary congestion [[15].]

5) **Hyperglycemia (serum glucose)** – It has been reported in many studies. The increase in serum glucose is due to secondary release of catecholamines from the adrenal medulla [14].
6) **Serum Amylase –** Many case reports have shown a rise in serum Amylase level following ingestion of organophosphorus poison with or without the development of Pancreatitis.
7) **Leukocyte Number** – Leucocytosis is a common finding in OP intoxication. It helps to assess the prognosis and efficiency of treatment [17].

Imaging Studies

Chest X-ray

For evaluating pulmonary edema (or) congestion.

CT/USG Abdomen to evaluate the pancreatic status.

CT scan of the head may be considered for patients with altered mental status [15].

Other Tests

Electrocardiogram (ECG)

Useful for evaluating the rare dysrhythmias including atrial fibrillation, ventricular tachycardia and torsades de pointes (or) QT prolongation.[18]

Treatment

Organophosphate poisoning is a serious condition that needs rapid diagnosis and intensive care support. Patients who receive appropriate treatment immediately recover from acute toxicity.

The main – stays of treatment are,

- Supportive care
- Atropine
- Oximes
- Benzodiazepines

The supportive care treatment includes

* Gastric lavage
* Air way control
* Oxygenation
* Ventilation and
* Seizure management.

2.5. DRUG THERAPY

Atropine:-

Category: - Physiologic antidote for antagonizing the muscarinic receptor mediated response.

Atropine antagonizes the excess AChE activity at muscarinic receptor mediated responses such as increased tracheobronchial secretions, excessive salivation and bronchoconstriction, but does not block nicotinic receptors hence a poisoned patient may have respiratory muscle – paralysis [19].

Full and early atropinisation is an essential and simple part of an early management and a delay can result in death from central respiratory depression, bronchospasm, bronchorrhoea, severe bradycardia or hypotension [20].

Targeted End – Points of Atropinisation [21].

- Clear lungs
- Dry axillae
- Systolic BP > 80mm Hg.
- Heart rate > 80 /min
- No miosis

Table 5. Atropine recommendations in major text books of internal medicines and national formularies [20]

Source	Recommended Regimen to attain Atropinisation	Marker of Atropinisation
Australian Medicines hand book 14th Edition, 2003.	2 mg IV repeated until Atropinisation is achieved then infusion titrated against clinical effects.	Abolish all secretions.
British National Formulary Edition - 46, 2003	2 mg repeated every 5 – 10 min. IM (or) I.V according to severity.	Dry Flushed skin, Dilated pupils, tachycardia
Harrison's Internal Medicine Edition - 16, 2005	0.5 – 2mg repeated every 5-15 min.	Dry secretions.
WHO model formulary Edition - 1, 2002	2 mg repeated every 20-30 min	Flushed early skin and tachycardia

Atropine Toxicity:-

Excess atropine can cause atropine toxicity characterized by confusion, agitation, atropine induced hyperthermia and cardiac arrest [20].

Oximes:

Category: Cholinesterase Reactivators.

Oximes are effective in treating nicotinic symptoms by reversing the phosphate – ester bond formed between the OP and acetyl cholinesterase and these reactivates the enzyme. It also prevents subsequent binding of insecticides to the AChE and accentuates therapeutic effects of atropine [25].

The oximes used are,

- Pralidoxime (Currently and commonly used)
- Obidoxime
- Trimedoxime
- Asoxime [10].

Oximes are indicated in muscle weakness (especially respiratory muscle paralysis). They must be used early in course of poisoning to be effective before the OP – AChE bond as aged. It may help to prevent intermediate and delayed neuromuscular and neuropsychiatric OP syndromes [15].

The WHO recommended pralidoxime regimen is 30 mg/kg bolus followed by 8 mg kg/hr infusion [1].Traditional dosing for pralidoxime in op poisoning is 1 gm every 8 – 12 hrs in adults and 25- 50 mg/ kg in children [22]

Benzodiazepines:-

Category: - antiepileptic, CNS depressant and anxiolytic.

It depresses all levels of CNS activities and is also used to treat OP – induced muscle fasciculations.

Dose Regimen: Adults: 10 – 20 mg 1.V,

Elderly: 5-10mg/1V

Children: 0.2 -0.3 mg/kg I.V [15].

2.6.1 .EFFECT OF ORGANOPHOSPHORUS COMPOUND ON PANCREAS :-

Various studies show that there is increased incidence of Pancreatitis and its related complications after consumption of Organophosphorus compound when compared to general population. There is elevated serum Amylase level in these patients.

Though the exact mechanism for its occurrence is not known , the following mechanisms have been suggested .

a) OP insecticides increase the intraductal pressure and exocrine pancreatic flow.The increase in pressure leads to extravasation of pancreatic fluid. This increased pancreatic exocrine flow could be due to direct cholinergic hyperstimulation of pancreatic acinar and ductal cells .
b) Experimental data supports the view that these organophosphate anticholineesterase compouds cause a functional ductal obstruction at the same time as stimulation of pancreatic exocrine secretion.
c) There is pancreatic interstitial edema , acinar cell vacuolization , hyperamylasemia and hyperlipasemia following ingestion of OP poisoning.

2.6.2 EFFECTS OF ORGANOPHOSPHOROUS COMPOUND ON VARIOUS OTHER ORGANS :-

1) Effects on the Central Nervous System:

- Complex changes in higher intellectual functions such as memory, problem solving and the interpretation of data.
- Neuropsychological effects like impaired vigilance, reduced information processing and psychomotor speed, memory deficit, linguistic disturbances, depression, anxiety and irritability.

2) Altered Immunity to Infection:

OP – induced immunosuppression was associated with severe cholinergic stimulation probably from a direct action of ACh upon the immune system or it may be secondary to the toxic chemical stress associated with cholinergic poisoning. A marked impairment of neutrophil chemotaxis and greater frequency of upper respiratory tract infection was demonstrated in subjects exposed to OP in whom a significant decrease in both serum and RBC cholinesterase activity was observed.

3) Change in Metabolism and endocrine activity:-

The following changes have been observed in various studies

a) Changes in glucose metabolism and in diurnal pattern of plasma ACTH
b) Non ketotic hyperglycemia and glycosuria
c) Significant decrease in serum T_3 and T_4 concentrations and increased levels of TSH.

d) Damage to seminiferous tubules and to the principal cells in caput epididymis through its toxic effect on the leydig cells.

4) Effects on cardiac function:-

Cardiac complications such as hypotension, hypertension, arrhythmias (Complete atrioventricular block, premature ventricular complexes, 'torsade de pointes' and cardiac arrest, often follow OP poisoning.

5) Effect on Reproduction:-

Op poisoning during pregnancy causes prenatal and postnatal death and congenital abnormalities such as vertebral deformities, limb defects polydactyly, intestinal hernia, cleft palate and hydroureter.

6) Miscellaneous effects:-

Inhibition of carboxyesterase enzymes especially, NTE, a brief bilateral vocal cord paralysis, arthritis, cerebellar disorder like ataxia [4].

2.7. STUDIES ON EFFECT OF OP COMPOUNDS ON SERUM AMYLASE LEVELS :

- A prospective study was done by the Department of Internal Medicine, University of Yuzuncu Yil,Medical faculty,Van,Turkey in 2002[37] to find the prevalence of pancreatitis in OP poisoning. Four of the total 47 patients with acute OP poisoning had obviously elevated Amylase and Lipase levels (Amylase > 300 U/L ; Lipase >60 U/L). Only two of the patients with Amylase levels between 100 and 300 U/L Had elevated levels of Lipase. None of the patients

with normal Amylase levels had elevated levels of Lipase. A total of 12.76% was diagnosed as acute Pancreatitis. It was concluded that acute Pancreatitis is not a rare complication of organophosphorus poisoning. In order to improve the outcome of OP poisoning early diagnosis of acute pancreatitis is important and serum Amylase and Lipase levels should be routinely considered carefully.

- A prospective study was undertaken in PGIMER,CHANDIGARH, INDIA between June 2001-June 2005[38] to find the incidence of hyperamylasemia and acute pancreatitis in patients with OP poisoning. Of the 79 patients studied, serum Amylase was found to be elevated (> 200 S.U) in 37 patients(46.95%). Among them in three patients it was 800 S.U. One of them showed swollen pancreas on ultrasonography and confirmed by CT. In other two patients, evidence of pancreatitis was not observed. There was no significant correlation between the nature of compounds (OP or carbamates), duration and severity of cholinergic syndrome and increase in serum Amylase. It has been concluded that mild elevation of serum Amylase is common in patients with OP poisoning, however acute Pancreatitis is rare.
- A case was reported by the Department of Internal Medicine ,Limassol General Hospital,Ciprus(dated 2005 March) [39]regarding severe acute pancreatitis following N-Methyl carbamate insecticide ingestion. An 18 year old Caucasian man was admitted in ICU with Cholinergic crisis after ingestion of a carbamate insecticide. Two days after admission, an abdominal CT scan revealed blurring of the peripancreatic fat planes, inflammation and swelling of pancreas, and substantial amount of ascitic fluid in the left anterior pararenal space and pelvis.

Paracentesis and analysis of ascitic fluid demonstrated findings suggestive of pancreatic ascites. There have been no other evident predisposing factors for acute pancreatitis other than carbamate intoxication. 11 days after admission repeat CT can revealed the formation of intrapancreatic fluid collection. Patient was discharged in good physical condition after two weeks of admission. The follow-up abdominal CT scan performed one month later showed a significant reduction in size of intrapancreatic fluid. Conclusion of the study was that acute pancreatitis was not uncommon after organophosphate intoxication and carbamates share the same risk as OP pesticides.

- A retrospective study of medical records of 121 patients with the diagnosis of OP poisoning over three years was done in Veterans general hospital, National Yang-Ming University in 1998[40]. Serum amylase , pancreatic amylase, salivary amylase, lipase and cholinesterase levels and the clinical manifestations were analyzed. It was observed that 44 patients (36%) had hyperamylasemia (Amylase >360 U/L). Lipase was measured in 28 patients with hyperamylasemia ; nine of 28 had hyperlipasemia (Lipase > 380 U/L). The finding of hyperamylasemia was closely related to clinical severity and presence of shock. It was concluded that hyperamylasemia is frequent in severe OP poisoning. However, hyperamylasemia is not synonymous with acute pancreatitis and pancreatic amylase is not reliable parameter in the diagnosis of organophosphate induced pancreatitis due to its low sensitivity and specificity. Lipase assay is indicated in patients with hyperamylasemia for early diagnosis of pancreatitis.

- A case report published in 1994 by Moritz F et al ,Reanimation medicale, Rouen, France [41]: A 29 year old woman was admitted for ingestion of carbamate insecticide. Cardiorespiratory arrest occurred at the second hour and acute necrotic hemorrhagic pancreatitis on the second day. Further evaluation was uneventful and the patient was discharged after 43 days. Carbamate intoxication was confirmed by high urinary Aldecarb metabolite concentrations. Hence, Carbamate pesticides carry the same risk as OP pesticides and should be monitored similarly.
- Surgical gastroenterology department, South Africa reported two cases of severe acute pancreatitis complicated by pancreatic necrosis and retroperitoneal sepsis in 1997[42]. Awareness of this complication should prompt earlier investigation because early diagnosis coupled with timely therapeutic measures may improve patients prognosis.
- A retrospective study of OP poison in intensive care unit was performed to analyze the incidence of respiratory failure by Department of Anesthesiology & Critical care medicine, Kyodo general hospital , Ibaraki ,Japan[43] . Of the 32 op poisoning Patients, 16 developed respiratory failure and received ventilatory support . An increase in plasma Amylase above the normal range was found in patients who developed respiratory failure. Thus in OP poisoning, the elevation of Amylase levels was predictive of subsequent respiratory failure.

AIM OF STUDY

3. AIM OF THE STUDY

(i) To estimate serum Amylase levels in acute organophosphorus compound poisoning.

(ii) To find out its relationship with

a) clinical severity

b) outcome

MATERIALS AND METHODS

4. MATERIALS AND METHODS

Subjects: Patients presenting with Organophosphorous poisoning were the study subjects.

Study design: A prospective cross - sectional study.

Ethical committee approval: The Ethical committee approval was obtained to carry out the study in the hospital.

Study setting: Government Rajaji Hospital Madurai.

Study duration: June 2007– June 2008

Materials:

Of a total of 145 patients with organophosphorus compound poisoning admitted to the hospital during the study period,40 were included in the study.

Controls :

10 healthy (age matched) individuals were kept as control.

Study criteria :

Inclusion criteria:

40 patients with a history of exposure to OP poison were the study subjects.

Exclusion criteria:

- Patients with indication of exposure to a entirely different poison other than OP poison.
- Patients with double poisoning

- Patients who have consumed poison along with alcohol
- Patients who are chronic alcoholics
- Patients with history suggestive of gall stone disease
- Patients with known history of lipid disorders
- History suggestive of parotid gland disease
- Patients with history of lipid disorders
- History suggestive of parotid gland disease
- Patients with history of renal or hepatic disease
- History of renal or hepatic disease
- History of intake of drugs likely to produce pancreatitis –

    Azathioprine

    6-Mercaptopurine

    Thiazides

    Frusemide

    Pentamidine

Study protocol:

Patients admitted in GRH were the study group. A previously designed proforma was used to collect the demographic and clinical details of the patients.

Collaborating department:

Department of Biochemistry, Madurai Medical College, Madurai

Exposure assessment:

The following parameters were analyzed for association with OP pesticide exposure.

- Demography
  - Age
  - Sex
  - Time of Admission
  - Economical Status
  - Familial Status
  - Reason for consumption
- Poison Particulars
  - Severity grade
  - Symptoms after consumption
  - Immediate steps taken after OP exposure
- Biochemical evaluation which includes Serum Amylase
  - Blood glucose, urea, creatinine and Liver function tests.
- Clinical Outcome ,Clinical Presentations
  - Pupil size, Pulse rate/min, Blood pressure, Respiratory rate/min, Secretions.

Sample collection:

40 Patients satisfying the inclusion criteria were selected for the study. About 3 ml of venous blood were collected in two occasions from each subject first within 24 hours of consumption of poison (Sample I) and next after 24 hours of first sample (Sample II). The samples were centrifuged at 3000 rpm for 15 minutes. The supernatant

serum was separated and freezed. Serum Amylase was estimated with the help of kit manufactured by Diasys Diagnostic Systems GmbH Alte S Strasse g 65558 Holyheim Germany by using CNP-G3 method Autoanalyser AUTOPAK.

Limitations of this study :

a) In this present study, patients were not subjected to CT / USG Abdomen because the study was limited to serum Amylase only.
b) Autopsy study of pancreas was not done in the view of social limitation.
c) Subsets of Amylase such as pancreatic and salivary Amylase was not estimated due to laboratory constraints.
d) Urinary Amylase was not estimated due to technical limitations.
e) Other biochemical parameters related to pancreatic involvement was not attempted due to financial constraints.

STATISTICAL ANALYSIS :

Data analysis was done with the help of computer using **Epidemiological Information Package (EPI 2002).**

Using this software, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's test for qualitative variables. A 'p' value less than 0.05 is relationship..

OBSERVATION AND RESULTS

5. OBSERVATION & RESULTS

A. CHARACTERISTICS OF CASES STUDIED

Table 1 : Age distribution

Age Group	Cases		Controls	
	No.	**%**	**No.**	**%**
Upto 20 years	5	12.5	1	10
21-30	16	40	3	30
31-40	14	35	4	40
41 & above	5	12.5	2	20
Total	40	100	10	100
Mean S.D.	32.3 yrs 9.3 yrs		29.9 yrs 9.5 yrs	
'p'	0.3558 Not significant			

AGE DISTRIBUTION

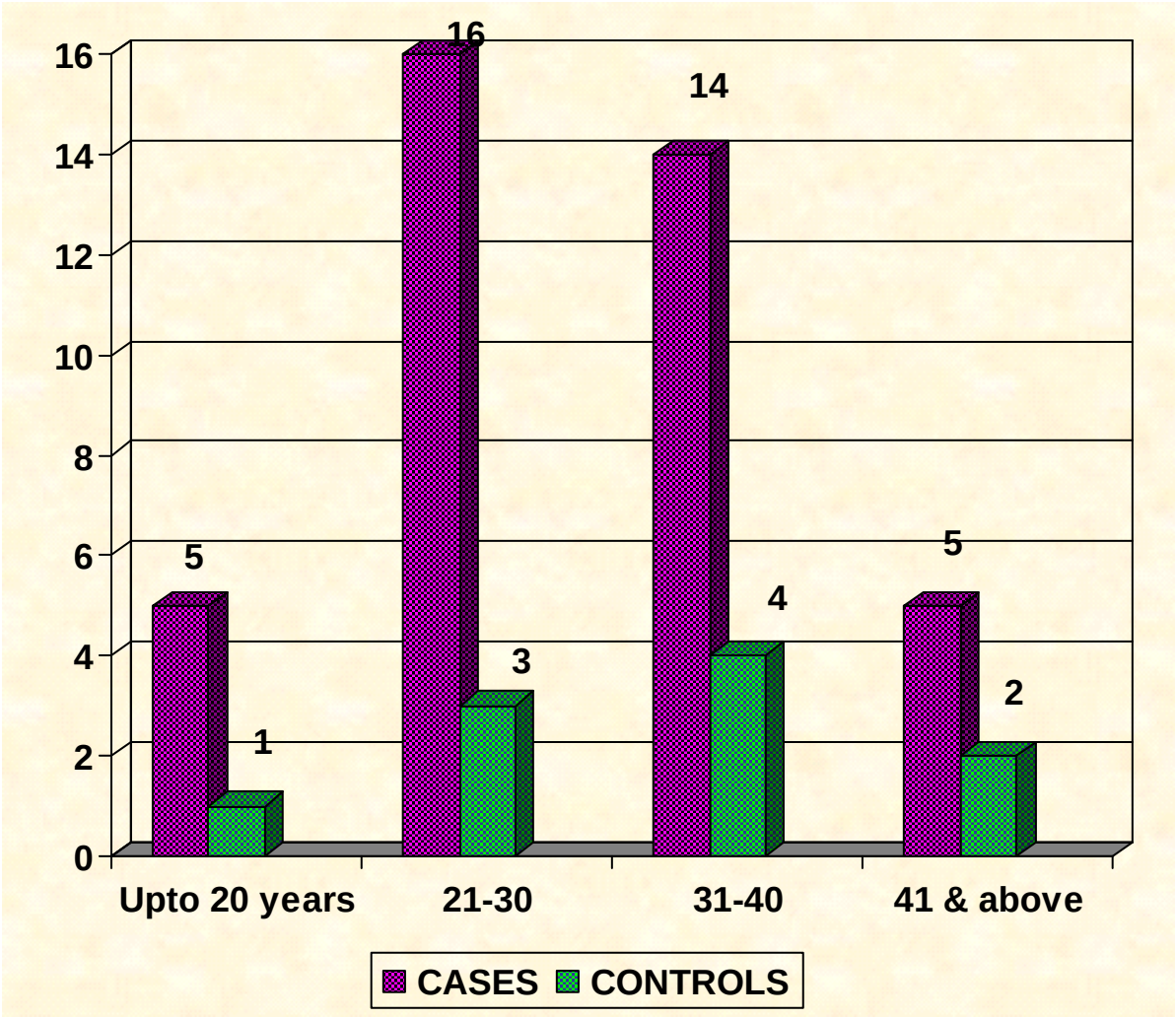


Table 2 : Sex

Sex	Cases		Controls	
	No.	%	No.	%
Males	26	65	7	70
Females	14	35	3	30
'p'	0.5395 Not significant			

SEX DISTRIBUTION

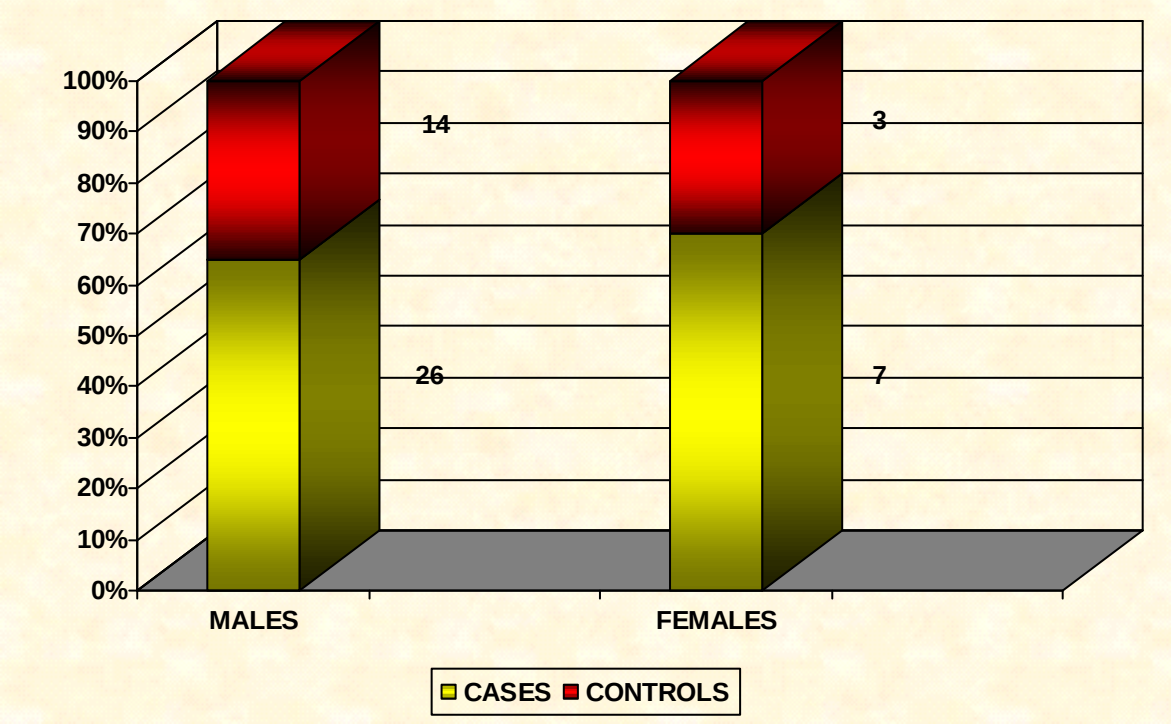


Table 3: Haematological parameters

Parameter	Cases		Controls		'p'
	Mean	S.D.	Mean	S.D.	
Blood sugar	96.9	24.2	102.3	11.2	0.2535 Not significant
Blood urea	29.8	7.4	31.4	5.0	0.5035 Not significant
Serum Creatinine	0.95	0.3	0.83	0.21	0.281 Not significant

B. FEATURES OF POISONING

Table 4 : Reason for poisoning

Reasons	Cases	
	No.	%
Familial	26	65
Financial	10	25
Job stress	2	5
Others	2	5
Total	40	100

REASONS FOR POISONING

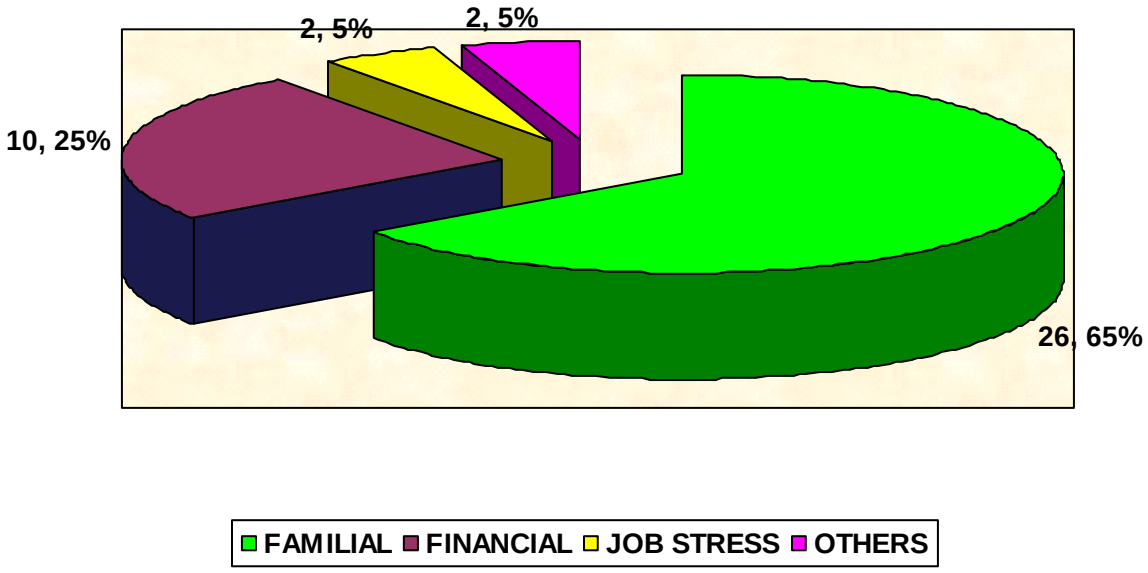


Table 5 : Mode of consumption

Mode of consumption	Cases	
	No.	%
Water	27	67.5
Milk	3	7.5
Alone	10	25
Others	-	-
Total	40	100

MODE OF CONSUMPTION

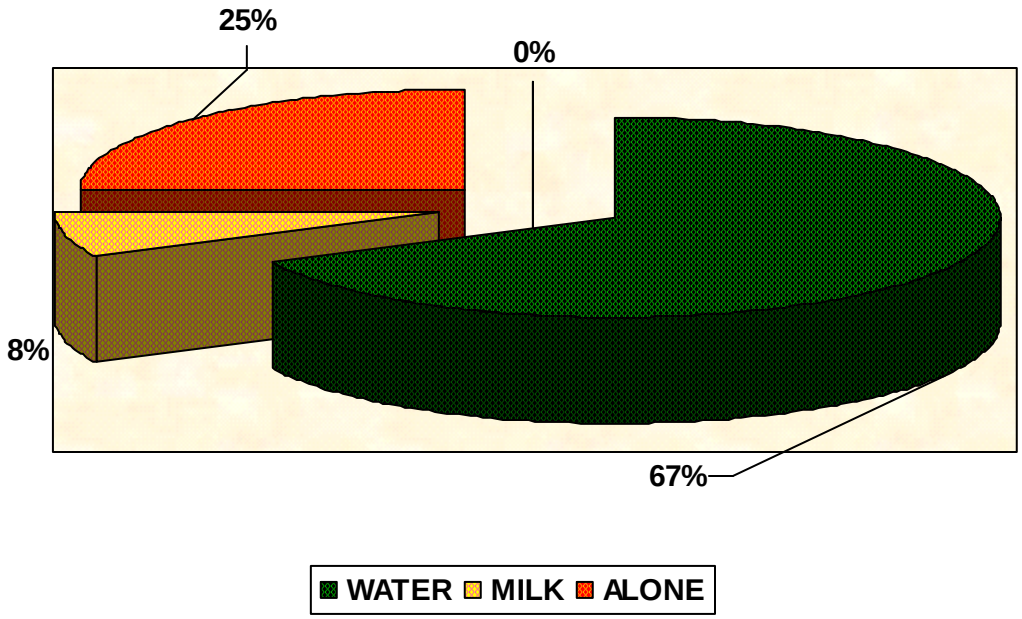


Table 6: Agents

Agents	Cases	
	No.	%
Methyl Parathion	21	52.5
Bug killer liquid	6	15
Fenthion	2	5
Quinolphos	4	10
Monocrotophos	2	5
Chlorpyrifos	4	10
Dichlorofos	1	2.5
Total	40	100

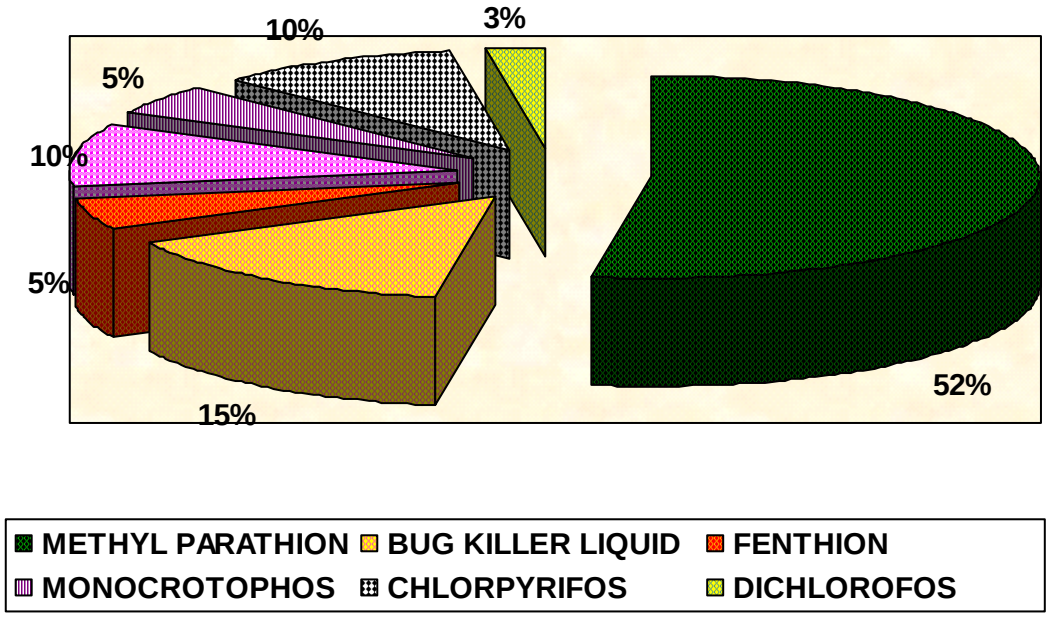
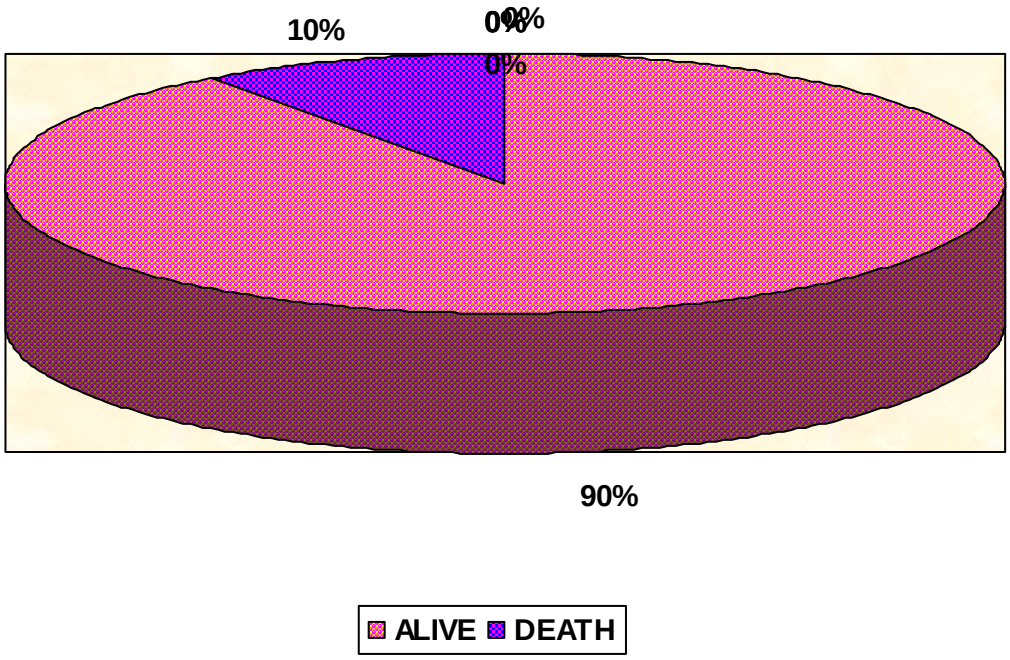


Table 7 : Clinical features

Clinical features	Cases	
	No.	**%**
Pinpoint pupil	22	55
Depressed mental status	11	27.5
Secretions		
i) Mild	3	7.5
ii) Moderate	24	60
iii) Severe	11	27.5
iv) NS	2	5
Fasciculation	12	30
Heart Rate		
i) Bradycardia	17	42.5
ii) Tachycardia	-	-
iii) Normal	23	57.5
Convulsions	1	2.5
Respiratory Failure	10	25

Table 8: Outcome

Outcome	Cases	
	No.	%
Alive	36	90
Death	4	10



RELATIONSHIP BETWEEN INCREASED AMYLASE LEVELS AND OTHER FACTORS

Table 9 : Increased Amylase levels in first 24 hours

Amylase levels in	Normal		Increased	
	No.	%	No.	%
Cases	15	37.5	25	62.5
Controls	10	100	-	-
'p'	0.0015 Significant			

AMYLASE LEVELS IN CASES & CONTROLS

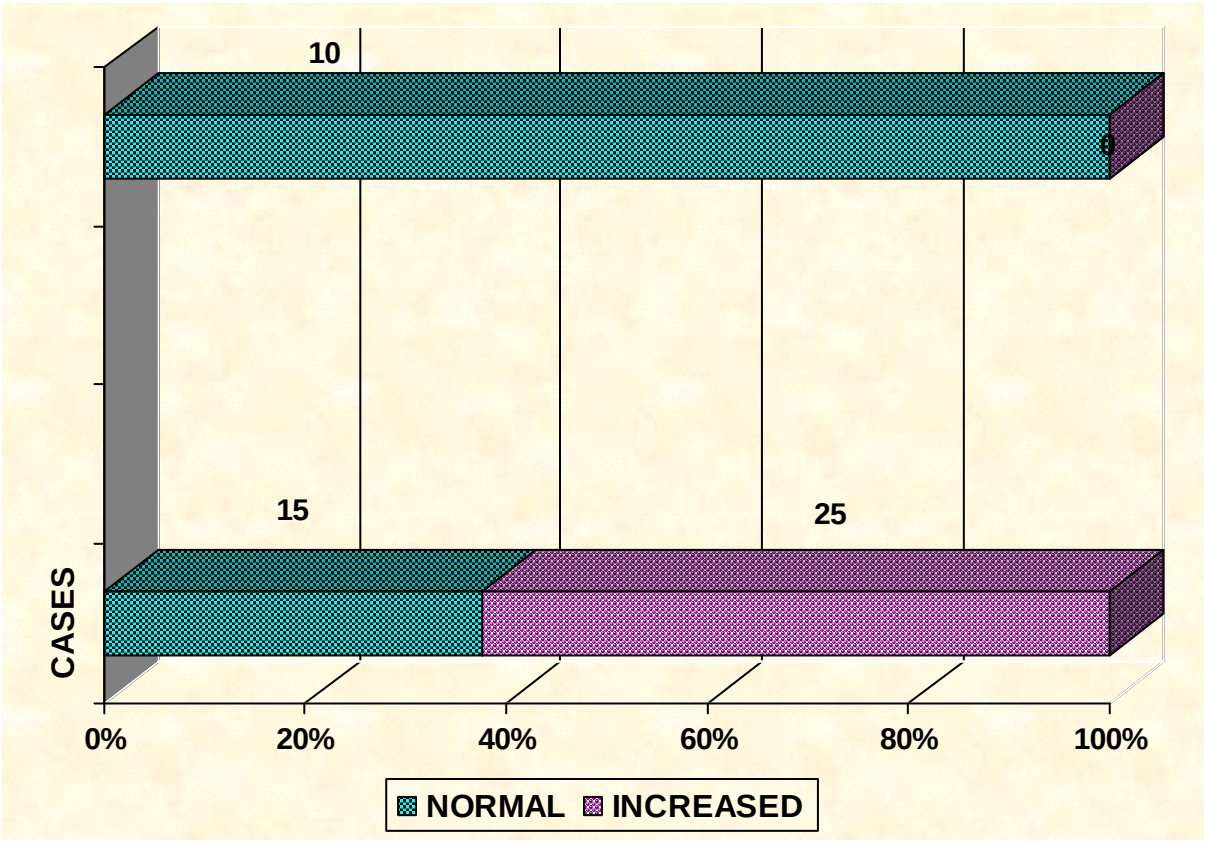


Table 10 : Age and Amylase levels

Age group	Amylase levels					
	I		II		I – II	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Upto 20 years	132.8	155.7	44.8	44.8	88	111.6
21-30	142.9	128.7	36.4	30.3	106.4	105.8
31-40	162.6	135.1	46.4	35	116.1	112.7
41 & above	94	28.6	30.8	22.4	63.2	17.5
'p'	0.7042 Not Significant		0.744 Not Significant		0.7146 Not Significant	

\

Table 11 : Sex and Amylase levels

Sex	Amylase levels					
	I		II		I – II	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Males	149.8	120.5	40.6	33.9	109.3	97.8
Females	128.6	134.9	39.7	30.9	88.9	108.4
'p'	0.321 Not Significant		0.876 Not Significant		0.3073 Not Significant	

Table 12 : Mode of consumption and Amylase levels

Mode of consumption	Amylase levels					
	I		II		I – II	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Water	137.7	103.4	41.5	31.7	96.1	84
Milk	41	27.2	15.3	3.8	25.7	25.7
Alone	185.6	174.5	44.4	37.6	141.2	140.2
'p'	0.0793 Not Significant		0.2074 Not Significant		0.0711 Not Significant	

Table 13 : Agents and Amylase levels

Agents	Amylase levels					
	I		II		I – II	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Methyl Parathion	150.4	157.4	39.3	35	111.1	127.5
Bug killer liquid	125.2	98.5	44.5	39.4	80.7	85.6
Fenthion	96	106.1	34.5	24.7	61.5	81.3
Quinolphos	172.5	52.3	51.8	37.1	120.8	21.7
Monocrotophos	148	141.4	45	46.7	103	94.8
Chlorpyrifos	120	48.9	32.5	13.2	87.5	47.6
Dichlorofos	128	-	22	-	106	-

Table 14 : Clinical features and Amylase levels

Clinical features	Amylase levels					
	I		II		I – II	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Pinpoint pupil						
Present	204.1	136.1	52.4	33.2	151.1	111.8
Absent	67	38.5	25.4	25.1	41.6	27.6
'p'	**0.0001 Significant**		**0.0009 Significant**		**0.0001 Significant**	
Depressed mental status						
Yes	261	151.8	63	31	198	131.1
No	97.4	75.6	31.7	29	65.8	54.9
'p'	**0.0003 Significant**		**0.0023 Significant**		**0.0004 Significant**	
Secretions						
v) Mild	83	59.2	30.3	25.7	52.7	33.8
vi) Moderate	108.9	90.6	30.3	26.8	78.6	67.4
vii) Severe	242.2	157.5	59.7	32.3	182.5	135.2
viii) NS	84.5	72.8	67.5	67.2	17	5.7
'p'	**0.0168 Significant**		**0.0219 Significant**		**0.0062 Significant**	
Fasciculation						
Present	272.3	149.9	67.5	33.4	204.8	127.2
Absent	86.6	50.8	29	24.7	57.6	17.5
'p'	0.0001 Significant		0.0001 Significant		0.0001 Significant	

Table 14 : Clinical features and Amylase levels (continued)

Clinical features	Amylase levels					
	I		II		I – II	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Heart Rate						
iv) Bradycardia	209.1	142.8	51.1	31.8	157.9	119.5
v) Tachycardia	-	-	-	-	-	-
vi) Normal	93.3	83.4	33	31.7	60.4	59.8
'p'	**0.0001 Significant**		**0.0321 Significant**		**0.0001 Significant**	
Convulsions						
Present	156	-	38	-	118	-
Absent	142.1	126.9	40.3	32.9	101.7	102
'p'	-		-		-	
Respiratory Failure						
Yes	297.7	151.8	69.8	36.4	227.9	126.7
No	90.6	50.8	30.4	24.6	60.2	37.3
'p'	**0.0001 Significant**		**0.0016 Significant**		**0.0001 Significant**	

CLINICAL FEATURES & AMYLASE LEVELS AT FIRST 24HOURS

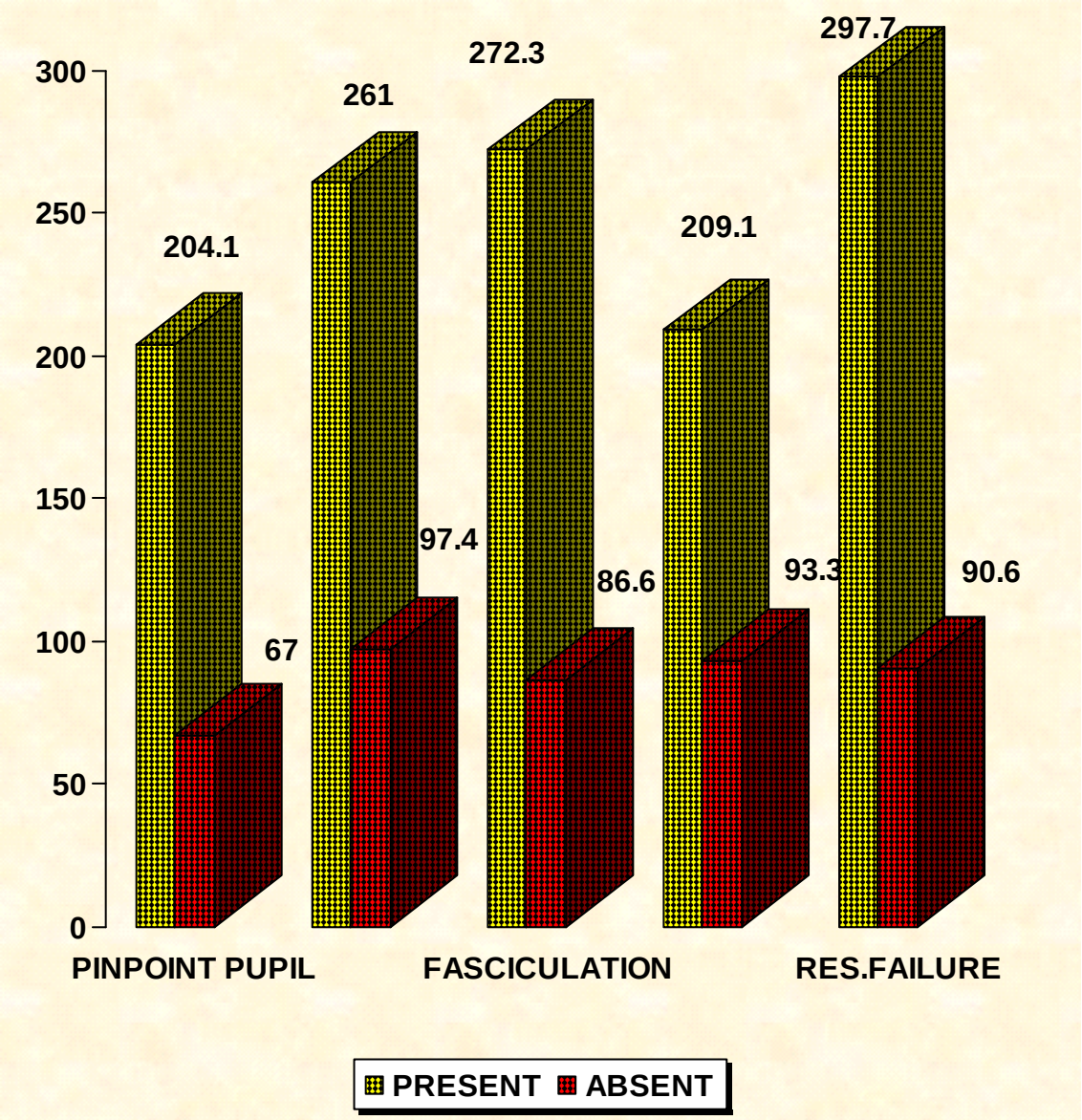


Table 15 : Outcome and Amylase levels

Outcome	Amylase levels					
	I		II		I – II	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Alive	134.6	122	39.9	33.4	94.7	96.3
Dead	213	142	44	25.3	169	130.7
'p'	0.1762 Not Significant		0.443 Not Significant		0.1428 Not Significant	

RELATIONSHIP BETWEEN OUTCOME AND VARIOUS PARAMETERS

Table 16 : Age and outcome

Age group	Alive		Dead	
	No.	**%**	**No.**	**%**
Upto 20 years(5)	5	100	-	-
21-30(16)	13	81.3	3	18.2
31-40(14)	13	92.9	1	7.1
41 & above(5)	5	100	-	-
Mean S.D.	30.4 years 9.7 years		25.5 years 5.1 years	
'p'	0.2783 Not Significant			

Table 17: Sex and outcome

Sex	Alive		Dead	
	No.	%	No.	%
Male(26)	23	88.5	3	11.5
Female(14)	13	92.9	1	7.1
'p'	0.5619 Not Significant			

Table 18: Reasons and outcome

Reasons	Alive		Dead	
	No.	%	No.	%
Familial(26)	22	84.6	4	15.4
Financial(10)	10	100	-	-
Job stress(2)	2	100	-	-
Others(2)	2	100	-	-

Table 19: Agents and outcome

Agents	Alive		Dead	
	No.	%	No.	%
Methyl Parathion(21)	18	85.7	3	14.3
Bug killer liquid(6)	6	100	-	-
Fenthion(2)	2	100	-	-
Quinolphos(4)	4	100	-	-
Monocrotophos(2)	1	50	1	50
Chlorpyrifos(4)	4	100	-	-
Dichlorofos(1)	1	100	-	-

Table 20: Mode of consumption and outcome

Reasons	Alive		Dead	
	No.	%	No.	%
Water(27)	23	88.2	4	14.8
Milk(3)	3	100	-	-
Alone(10)	10	100	-	-

Table 21: Haematological parameters and outcome

Parameter	Cases		Controls		'p'
	Mean	S.D.	Mean	S.D.	
Blood sugar	97.2	23.5	94	33.7	0.5419 Not Significant
Blood urea	29.4	6.8	33	13.2	0.4976 Not Significant
Serum Creatinine	0.95	0.32	0.98	0.19	0.6578 Not Significant

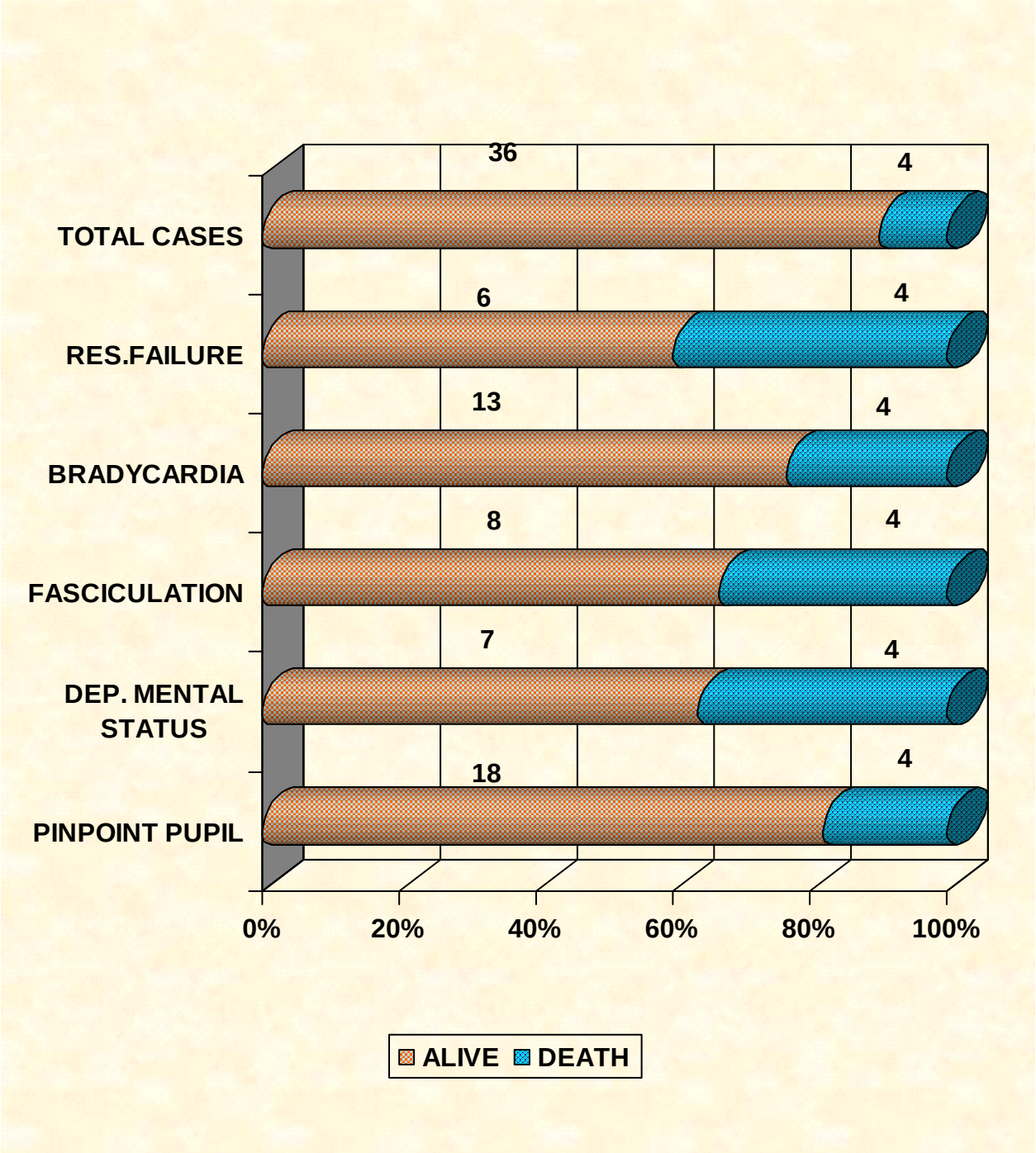
Table 22: Clinical parameters and outcome

Clinical features	Outcome				'p'
	Alive		Death		
	No.	No.	No.	No.	
Pinpoint pupil					
Present(22)	18	81.8	4	18.2	0..8
Absent(18)	18	100	-	-	Not significant
Depressed mental status					
Yes(11)	7	63.6	4	36.4	**0.0036**
No(29)	29	100	-	-	**Significant**
Secretions					
ix) Mild(3)	3	100	-	-	**0.0001**
x) Moderate(24	24	100	-	-	**Significant**
xi) Severe(11)	7	63.9	4	36.4	
xii) NS(2)	2	100	-	-	
Fasciculation					
Present(12)	8	66.7	4	33.3	**0.0054**
Absent(28)	28	100	-	-	**Significant**

Table 22 : Clinical features and Outcome (continued)

Clinical features	Outcome				'p'
	Alive		Death		
	No.	%	No.	%	
Heart Rate					
vii) Bradycardia(17)	13	76.5	4	23.5	**0.026**
viii) Tachycardia(-)	-	-	-	-	**Significant**
ix) Normal(23)	23	100	-	-	
Convulsions					
Present(1)	-	-	1	100	0.1
Absent(39)	36	92.3	3	7.7	Not significant
Respiratory Failure					
Yes(10)	6	60	4	40	**0.0023**
No(30)	30	100	-	-	**Significant**

CLINICAL FEATURES & OUTCOME



DISCUSSION

6. DISCUSSION

Organophosphates and Carbamates are frequently used pesticides which can produce life-threatening intoxication. Well over 50,000 organophosphorous compounds have been synthesized since the first one by Clermont in 1857. All these compounds act by irreversible inactivation of acetylcholinesterase (ACh). The clinical symptoms range from the classic cholinergic syndrome to flaccid paralysis and intractable seizures. About 99% of fatal poisoning occurs in developing countries, particularly among farm workers. Despite an increased incidence of organophosphorous insecticide poisoning, the exact micro molecular changes that take place remain elusive. Till date, atropine and oxime continue to occupy the prime position in the specific management of OP poisoning.

With the ease of availability, it is not surprising that the use of OP compounds in suicide attempts has mushroomed from a disturbing early trend to being one of the commonest modes of suicidal poisoning which accounted for 100% in our study. This rate was consistent with the findings of Mahadi Balali Mood et al [38] (94.3%) whereas it was reported to be 67% by AM Saadeh et al [18]. There was no accidental exposure in our study. This alarming incidence of suicidal attempts, may be probably because of the uncontrolled sale and use of these agents all over the country.

Age, Gender Prevalence

The vast majority of poisonings followed oral ingestion of liquid form and almost for all the patients gastric lavage was immediately done. The incidence was higher (40%) in the age group of 21-30 followed by (35%)in the age group of 31-40.

These are consistent with the findings of Muhammet Guven et al [17] and AM Saadeh et al [18] , where the mean ages were 24.1 and 23.95 respectively.

The most common reason for consumption in our study was found to be the familial stress (65%) followed by financial stress (25%). Methyl parathion accounted for about 52.5% of intoxication .The commonest mode of intake was found to be poison along with water (67.5%).

Clinical symptoms

The accumulation of ACh in nerve terminals, results in continued stimulation with subsequent paralysis of receptors and accounts for the clinical signs of muscarinic, nicotinic and CNS effects.

Both the present study, and the study by Mahdi Balali-Mood et al [38], found association between the severity of poisoning and clinical manifestations. The most marked muscarinic signs in our study population were, miosis (55%), excessive secretions (60%), and respiratory distress (25%). The most prominent of the nicotinic effect is muscular end plate block, resulting in muscle weakness and fasciculations (30%). The CNS symptoms, like depressed mental status was found in (27.5%) patients. Similar findings have also been reported by Murat Sungur et al [14].

Biochemical evaluation

The biochemical (Blood sugar, Serum creatinine & urea) results have not shown much variation from the normal levels in our study which was also indicated by Mahdi Balali-Mood et al [38].

Respiratory Depression

The most troublesome complication of OP poisoning was respiratory depression which could be due to reasons such as: aspiration of gastric contents, excessive secretions, pneumonia and septicemia complicating adult respiratory distress syndrome. Of the 40 patients, respiratory depression was observed in 10 (25%) cases.

Early recognition of respiratory failure, prompt endotracheal intubations and mechanical ventilation are life saving in severe OP poisoning.

Serum Amylase levels in OP poisoning

OP insecticides increase the intraductal pressure and exocrine pancreatic flow. The increase in pressure leads to extravasation of pancreatic fluid. This increased pancreatic exocrine flow could be due to direct cholinergic hyperstimulation of pancreatic acinar and ductal cells .

In the study, the Amylase levels were significantly elevated at the time of admission [185.2 U/L] and have shown a gradual remission with proper treatment. The mean Amylase level in severely poisoned patients was 297.7 U/L which was significantly ($P < 0.01$) higher than the healthy control group.

On comparing the Amylase levels in first 24 hours against control, the variations were considered to be significant ($P < 0.01$).

From our observation, it can be suggested that estimation of Amylase levels would be extremely useful to assess the clinical severity .

Age and sex of the patients have no significant relationship with the amylase levels. The mean Amylase level in first 24 hours was 154 U/L which is significantly higher than the control groups.

In our study, there was no significant correlation between elevated Amylase levels and the outcome. From the observation we made, it could be suggested that OP pesticide poisoning is a serious condition that needs rapid diagnosis and treatment.

CONCLUSION

7. CONCLUSION

In India, Organophosphorus compounds cause more suicidal deaths among the earning and nonearning members of the society. Of the 40 patients in our study 15 patients (37.5%) had normal serum amylase level ; 25patients (62.5%) had elevated serum amylase level which is very significant.

From the observation we made, it could be suggested that OP pesticide poisoning is a serious condition that needs rapid diagnosis and treatment. The mean Amylase level in first 24 hours of OP poisoning was 154 U/L which is significantly higher than the control groups.

The bad bedside prognostic factors which correlated very well with serum Amylase levels in the order of increasing severity include

i) Convulsions (Amylase – 156 U/L)

ii) Severe secretions (242 U/L)

iii) CNS depression (261 U/L)

iv) Fasciculations (272U/L)

v) Respiratory failure (297.7U/L)

Hence Serum amylase levels may be considered as a marker of Organophosphorous intoxication, since it enables the early recognition of severity and also helps to identify those at risk of developing the complications of Organophosphorous poisoning .

Our study also showed that there was a significant correlation between markedly elevated Amylase level and respiratory failure and therefore poor outcome.

A significant rise in Serum Amyase level also portends various complications that include convulsions , CNS depression, fasciculations and respiratory failure.

However, as the study was limited to a small population due to financial and laboratory constraints, analysis of a larger group would definitely give an insight into the further finer relationship between serum amylase level and clinical severity and outcome in OP poisoning.

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APPENDIX

PROFORMA

NAME : **IP NO :**

AGE / SEX : **D.O.A :**

RESIDENCE : URBAN / RURAL **D.O.D :**

OCCUPATION :

INCOME :

TIME BETWEEN POISONING & ADMISSION :

SUICIDAL / ACCIDENTAL / HOMICIDAL

REASON :

TREATMENT PRIOR TO ADMISSION : YES / NO

POISON PARTICULARS :

NAME OF POISON - CHEMICAL NAME :

TRADE NAME :

QUANTITY CONSUMED :

NATURE OF POISON : LIQUID / POWDER / GRANULES

MODE OF CONSUMPTION :

IMMEDIATE STEPS TAKEN :

SYMPTOMS :

GIT: VOMITING

ABDOMINAL CRAMPS

ABDOMINAL PAIN / DISTENSION

DIARRHOEA

CNS: ALTERED SENSORIUM

SEIZURES

BLURRING OF VISION

FASCICULATIONS (TWITCHING)

PARALYSIS (WEAKNESS)

BREATHLESSNESS

OTHERS : SALIVATION / FROTHING

SWEATING

LACRIMATION

<u>PAST HISTORY :</u>

SIMILAR ATTEMPTS BEFORE : YES / NO

PREVIOUS PSYCHIATRIC ILLNESS : YES / NO

COMORBID ILLNESS : CARDIAC DISEASE

CHRONIC LUNG DISEASE

RENAL FAILURE

GALL STONE DISEASE

NEUROMUSCULAR DISEASE

H/O DRUG INTAKE

H/O JAUNDICE

H/O RECENT SURGERY

H/O ALCOHOL INTAKE

<u>CLINICAL PROFILE AT THE TIME OF ADMISSION :</u>

CONSCIOUSNESS **PR :**

PUPIL SIZE **BP :**

JAUNDICE **RR :**
CYANOSIS

FASCICULATIONS

CONVULSIONS

RS : SECRETIONS

RESPIRATORY INSUFFICIENCY

ABDOMEN : DISTENSION / TENDERNESS / PALPABLE MASS

BOWEL SOUNDS + / --

<u>INVESTIGATIONS :</u>

TC

DC

HB %

ECG

BLOOD SUGAR : **UREA :** **CREATININE :**

LIVER FUNCTION TESTS : SR.BILIRUBIN – TOTAL : **DIRECT :**

INDIRECT:

SGOT : **SGPT:** **ALP:**

PROTEIN-TOTAL: **ALBUMIN:** **GLOBULIN:**

SERUM AMYLASE : I :

II :

<u>COMPLICATIONS:</u>

RESPIRATORY FAILURE **HYPOTENSION**

HYPOKALEMIA **PANCREATITIS**

ARRYTHMIAS **HEPATOCELLULAR JAUNDICE**

DURATION OF HOSPITALIZATION :

FINAL OUTCOME : FULL RECOVERY **PARTIAL** **DEATH**

MASTER CHART

S. No	Age	Sex	Type of Exposure	Reason	Agents	Mode of Consumption	Clinical Features							Amylase Levels (IU/L)		Bl.S	Bl.U	Bl.C	Out come
							P	M	S	F	H	C	RF	I	II	Mg%	Mg%	Mg%	
1	20	M	I	Fa	MP	W	+	-	++	+	N	-	+	397	117	109	35	0.9	Alive
2	32	M	I	Fi	B	W	-	-	NS	-	N	-	-	136	115	79	42	1.3	Alive
3	22	M	I	Fa	MP	W	+	+	+++	+	B	-	+	391	43	84	16	0.7	Dead
4	33	M	I	Fa	F	M	-	-	++	-	N	-	-	21	17	88	19	1	Alive
5	24	F	I	Fa	MP	W	+	+	+++	+	B	+	+	156	38	63	32	1	Dead
6	35	M	I	Fi	C	W	+	+	+++	+	B	-	+	188	30	72	22	0.6	Alive
7	24	F	I	Fa	MP	W	-	-	++	-	N	-	-	15	10	68	30	0.7	Alive
8	24	M	I	Fa	D	W	+	-	++	-	B	-	-	128	22	102	21	1.1	Alive
9	31	F	I	Fa	MP	W	-	-	++	-	N	-	-	37	12	98	32	0.8	Alive
10	22	M	I	Fa	B	W	+	-	++	-	N	-	-	112	22	68	31	1.5	Alive
11	35	F	I	Fi	C	M	+	-	++	-	B	-	-	72	18	76	28	0.6	Alive
12	42	M	I	Fa	MP	W	-	-	++	-	N	-	-	98	15	64	25	1.5	Alive
13	23	M	I	Fa	MP	W	+	+	+++	+	B	-	+	57	17	87	48	1.1	Dead
14	16	F	I	Fa	B	W	-	-	NS	-	N	-	-	33	20	72	24	0.8	Alive
15	29	F	I	Fi	Q	W	+	+	+++	+	B	-	+	213	90	114	36	0.6	Alive
16	32	F	I	Fa	MP	A	+	+	+++	+	B	-	+	529	100	142	38	1.2	Alive
17	25	M	I	Fa	MP	W	-	-	++	-	N	-	-	75	19	96	25	0.5	Alive
18	35	M	I	O	MP	W	-	-	++	-	N	-	-	87	32	108	38	0.8	Alive
19	31	F	I	Fi	Q	W	+	-	++	-	N	-	-	217	77	60	20	0.9	Alive
20	16	F	I	Fa	MP	W	-	-	+	-	N	-	-	151	60	106	25	0.7	Alive
21	45	M	I	Fa	MO	A	+	-	++	-	B	-	-	48	12	98	32	1.1	Alive
22	55	M	I	Fa	MP	A	+	+	+++	+	B	-	-	120	60	72	23	0.9	Alive
23	38	M	I	Fa	MP	W	-	-	-	-	N	-	-	55	15	82	36	1.3	Alive
24	25	F	I	Fi	B	W	-	-	++	-	N	-	-	63	24	100	22	0.8	Alive
25	35	F	I	Fa	F	A	+	+	+++	+	B	-	-	171	52	110	38	1.3	Alive
26	25	F	I	Fa	MP	W	-	-	++	-	N	-	-	70	28	88	26	0.6	Alive
27	30	M	I	Fa	MP	W	+	-	++	-	B	-	-	178	70	98	30	1.1	Alive
28	23	F	I	Fi	MP	W	-	-	+	-	N	-	-	43	16	94	32	0.7	Alive
29	40	M	I	Fa	B	W	+	+	++	+	B	-	+	312	68	60	25	0.9	Alive
30	38	M	I	Fa	B	A	+	-	++	-	N	-	-	95	18	126	36	1.4	Alive
31	17	F	I	Fi	MP	M	-	-	++	-	N	-	-	30	11	104	40	1.8	Alive
32	23	M	I	J	C	A	+	-	+++	-	B	-	-	105	32	140	17	0.6	Alive
33	21	M	I	Fi	MP	A	-	-	++	-	N	-	-	42	13	98	34	0.6	Alive
34	16	M	I	Fa	MP	W	-	-	++	-	N	-	-	53	16	98	18	0.8	Alive
35	25	M	I	J	Q	A	+	-	++	-	B	-	-	152	22	106	34	1.2	Alive
36	33	M	I	Fa	MO	W	+	+	+++	+	B	-	+	248	78	142	36	1.1	Dead

S. No	Age	Sex	Type of Exposure	Reason	Agents	Mode of Consumption	Clinical Features							Amylase Levels (IU/L)		Bl.S	Bl.U	Bl.C	Out come
							P	M	S	F	H	C	RF	I	II	Mg%	Mg%	Mg%	
37	45	M	I	Fi	C	W	+	-	++	-	N	-	-	115	50	120	36	0.8	Alive
38	52	M	I	Fa	MP	W	-	-	++	-	N	-	-	89	17	130	28	O.6	Alive
39	28	M	I	O	MP	A	+	+	+++	+	B	-	+	486	117	156	32	1	Alive
40	31	M	I	Fa	Q	A	-	-	++	-	N	-	-	108	18	98	30	0.8	Alive
41	35	M	Control	-	-	-	-	-	-	-	-	-	-	32		84	30	0.8	
42	44	F	Control	-	-	-	-	-	-	-	-	-	-	24		110	36	1	
43	25	M	Control	-	-	--	--	-	-	-	-	-	-	28		96	38	1.1	
44	33	M	Control	-	--	-	--	-	-	-	-	-	--	36		108	28	0.6	
45	50	M	Control	-	-	-	-	-	-	-	-	-	-	26		117	38	1.2	
46	19	F	Control	-	-	-	-	-	-	-	-	-	-	22		86	28	0.6	
47	26	M	Control	-	-	-	-	-	-	-	-	-	-	35		98	26	0.8	
48	32	M	Control	-	-	-	-	-	-	-	-	-	-	40		110	24	0.6	
49	34	F	Control	--	-	--	-	-	-	-	-	-	-	45		102	34	0.8	
50	25	M	Control		--	-	-	-	-	-	-	-	-	46		112	32	0.8	

ABBREVIATIONS :

TYPE OF EXPOSURE

I	-	INTENTIONAL
A	-	ACCIDENTAL

REASON FOR CONSUMPTION

Fa	-	Familial
Fi	-	Financial
J	-	Job stress
O	-	Others

MODE OF CONSUMPTION

W	-	Water
M	-	Milk
A	-	Alone
O	-	Others

AGENTS

Mp	-	Methyl parathion
B	-	Bug killer liquid
F	-	Fenthion
Q	-	Quinolphos
Mo	-	Monocrotophos
C	-	Chlorpyrifos
D	-	Dichlorofos

CLINICAL FEATURES

P	-	Pinpoint pupil
M	-	Depressed Mental Status
S	-	Secretions + Mild ++ Moderate +++ Serere
F	-	Fasciculation
H	-	Heart Rate - B – bradycardia - T – Tachycardia - N – Normal
C	-	Convulsions
RF	-	Respiratory failure
Bl.S	-	Blood Sugar
Bl.U	-	Blood Urea
Sr.C	-	Serum Creatinine